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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/539,107	06/15/2005	Tomasz Heyduk	102364	2295
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EXAMINER				
BHAT, NARAYAN KAMESHWAR				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Advisory Action  
Before the Filing of an Appeal Brief**

<b>Application No.</b> 10/539,107	<b>Applicant(s)</b> HEYDUK ET AL.
<b>Examiner</b> NARAYAN K. BHAT	<b>Art Unit</b> 1634

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 12 May 2009 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.  
b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.  
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**NOTICE OF APPEAL**

2. ☐ The Notice of Appeal was filed on \_\_\_\_\_. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

**AMENDMENTS**

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because  
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);  
(b) ☐ They raise the issue of new matter (see NOTE below);  
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or  
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_ (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).  
5. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.  
6. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).  
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.  
The status of the claim(s) is (or will be) as follows:  
Claim(s) allowed: None.  
Claim(s) objected to: None.  
Claim(s) rejected: 109-111, 116 and 119-127.  
Claim(s) withdrawn from consideration: 112-115, 117 and 128-130.

**AFFIDAVIT OR OTHER EVIDENCE**

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).  
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).  
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

**REQUEST FOR RECONSIDERATION/OTHER**

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:  
See Continuation Sheet.  
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). \_\_\_\_\_.  
13. ☐ Other: \_\_\_\_\_.

/JD Schultz/  
Supervisory Patent Examiner, Art Unit 1635

Continuation of 11, does NOT place the application in condition for allowance because claims 109-111, 116, 119-122 and 124-127 have been rejected as being anticipated by Baez et al. Claims 109 and 123 have been rejected under 103(a) as being unpatentable over Baez et al and Zalipsky. Applicant's arguments filed on May 12, 2009 have been fully considered but they are not persuasive for the following reasons.

Claim rejections 35 USC 102 (b):

Applicant argues that Baez et al do not disclose R2/R6 or R3/R7 as required by claim 109 (Remarks, pg. 10, last paragraph). This argument is not persuasive because Applicant has asserted that biosensor of Baez et al teaches R2/R6 and R3/R7 (Remarks, Diagram 1B).

Applicant further argues that Baez et al do not teach a non- nucleic acid linker (Remarks, pg. 12, paragraph 1). This argument is not persuasive because as described in the final action in section 11, Baez et al teaches Sufo SMCC bifunctional chemical cross linker (paragraph 0165, lines 5-6 and paragraph 0169, line 3), and is the preferred R2 and R6 as defined in the instant claim 121. Furthermore, instant specification does not provide limiting definition for a "flexible linker". Therefore "flexible linker" is given broadest reasonable interpretation. Given the broadest reasonable interpretation, Sufo-SMCC linker of Baez et al meets the structural limitation of R2 and R6 as claimed. Since Baez et al teaches a bifunctional chemical crosslinker to link R1 and R3 and R5 and R7 as claimed remaining arguments regarding non-nucleic acid linker are not persuasive (Remarks, pgs. 12 and 13).

Applicants further argue that R2 of Baez et al comprises nucleic acid portion, hence Baez et al does not anticipate the claim 109 (Remarks, pg. 12, paragraphs 3 and 4). This argument is not persuasive for the same reasons as described above.

Applicant further argues that office interpretation of Baez et al has remarkably changed with different office action (Remarks, pg. 13, paragraphs 2 and 4). This argument is not persuasive because as described above "flexible linker" is given broadest reasonable interpretation because instant specification does not provide limiting definition for the "flexible linker". Given the broadest reasonable interpretation of the linker, the Sufo-SMCC linker comprising nucleic acid portion is a linker because there was no requirement for the non-nucleic acid portion of the linker in the claim at the time of the first office action. The Sufo-SMCC linker is a non-nucleic acid linker as required by the amended claim at the time of the final office action. The open claim language "comprising" encompasses both interpretations as recited in the claim at the time of the rejection. Therefore arguments are not persuasive.

Applicant further argues that the entire sequence of R3 and R7 of Baez et al are not complementary (Remarks, pg. 14, paragraph 1, and lines 1-2). This argument is not persuasive because claim 109 merely requires that R3 and R7 are pair of complementary sequence and not the "entire" sequence of R3 and R7 as Applicant asserts.

Applicant further argues that the entire nucleic acid label does not have a free energy of about 5.5. Kcal/mol to about 8.0 Kcal/mole (Remarks, pg. 14, paragraph 1, lines 3-4). This argument is not persuasive because claim 109 requires that R3 and R7 are pair of "complementary nucleotide sequences" having a free energy of about 5.5. Kcal/mole to about 8.0 Kcal/mole and not "across" the "entire sequence" that Applicant argues about. As described in the final office action in section 11, Baez et al teaches that R3 and R7 component of the R1-R2-R3-R4 and R5-R6-R7-R8 sensor have seven base pair complementary region at the 3' end and have a sequence CGCCCCGA (Table 1, paragraphs 0182-0183). As described in the final office action, using the HYTHER program, the CGCCCCGA sequence at 50 mM salt concentration and at a temperature of 37C has a free energy of association of 6.05 kcal/mol, which is in the range from about 5.5 kcal/mole to about 8.0 kcal/mole as claimed. Since Baez et al teaches the claimed free energy of association within the claimed range of temperature and the salt concentration, arguments are not persuasive.

Applicant further argues that 37C is the wrong temperature to evaluate Baez et al sequence because temperature of 25C is used to avoid duplex formation at 37C (Remarks, pg. 15, paragraph 3, pg. 16, paragraph 2). This argument is not persuasive because Baez et al teaches a plurality of embodiments wherein the temperature for incubation is between 25C and 45C (paragraph 0225) and temperature of 37C is within that range. Furthermore, Applicant has asserted that Baez et al's sensor has a free energy of 8.65 Kcal at 25C (Table C), which is "about" 8.0 Kcal as claimed. Since Baez et al teaches the sensor as claimed, arguments are not persuasive.

Applicant further states that regarding claim 119, he is not certain of the phrase regarding free energy of bonds formed as an "obvious variant" of the molecular sensor (Remarks, pg. 17, paragraph 2). Baez et al teaches the molecular sensor as claimed including the free energy of association between complementary R3/R7 sequences. Since the structural components of the sensor including all claimed bonds between R2 and R1 and R3 and R2 are taught by Baez et al, the free energy of the bonds formed in the molecular sensor is an obvious variant of the molecular sensor which does not further define the molecular sensor over the prior art (MPEP 2114).

Applicant's argument regarding claim 127 is directed to free energy of association between 5.5 Kcal to 8.0Kcal (Remarks, pg. 17, paragraph 3). This argument is not persuasive for the same reasons as described above.

Claim rejections 35 USC 103 (a):

Applicants further argue that Baez et al do not disclose a non-nucleic acid linker and Baez et al and Zalipsky do not teach PEG as a linker (Remarks, pg. 18, paragraphs 3 and 5). These arguments are not persuasive because as described above Baez et al teaches a non-nucleic acid linker. Furthermore, Applicant has asserted that Zalipsky teaches a PEG linker (Remarks, pg. 18, paragraph 5). Applicant has

not traversed the teachings, suggestion and motivation (TSM) of Zalipsky. Since Baez et al and Zalipsky teaches structural components of the sensor as claimed in claim 119, arguments are not persuasive.

Applicant further argues that there is no motivation to have non-nucleic acid linker in Baez et al and Baez et al actually teaches away from using a non-nucleic acid linker (Remarks, pg. 19, paragraph 1). This argument is not persuasive because as described above Baez et al teaches a non-nucleic acid linker and therefore argument regarding Baez et al teaching away from the non-nucleic acid linker is not persuasive.

Applicant further argues that there was no motivation to alter the Zalipsky reference (Remarks, pg. 19, paragraph 2). This argument is not persuasive because the sensor of Baez et al is lacking the PEG linker and Zalipsky provides TSM to incorporate the PEG linker into the sensor of Baez et al and not the other way around. For these reasons arguments are not persuasive.

Applicants further argue that prima facie case has not established (Remarks, pg. 19, paragraph 2). This argument is not persuasive because Applicants have asserted that Zalipsky teaches a polyethylene glycol linker. Baez et al and Zalipsky teach the structural components of the sensor as claimed. Therefore arguments are not persuasive.

#### Double Patenting

Applicants have not traversed the obviousness-type double patenting rejection. Therefore, provisional obviousness-type double patenting rejection of instant claims 109-111, 116, 119-127 over claims 1-11 of co-pending Application No. 11/836,339 are maintained.

For the reasons as cited above, provisional obviousness-type double patenting rejection of instant claims 109-111, 116, 119-127 over claims 1-8 of copending Application No. 11/836,333 are maintained. .